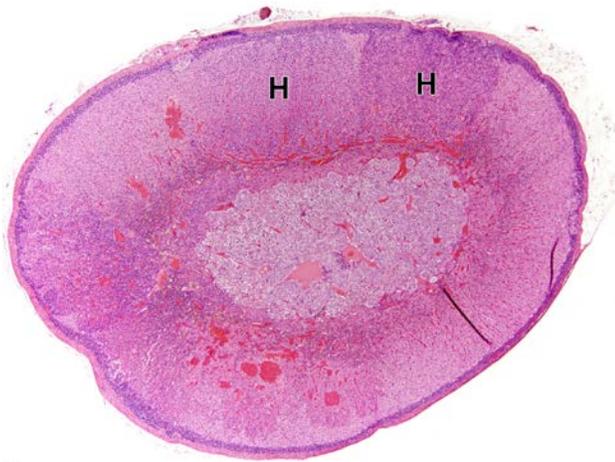
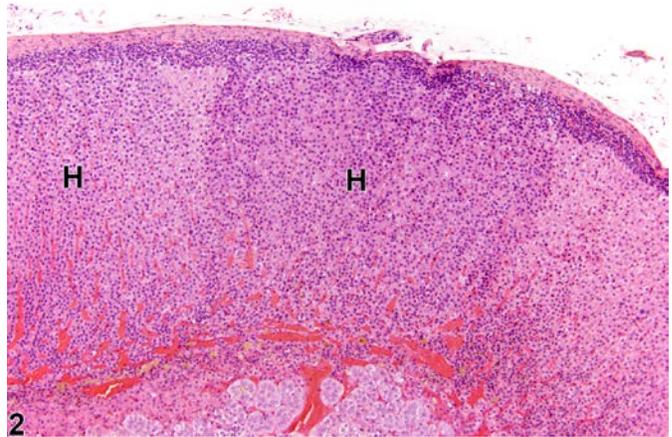


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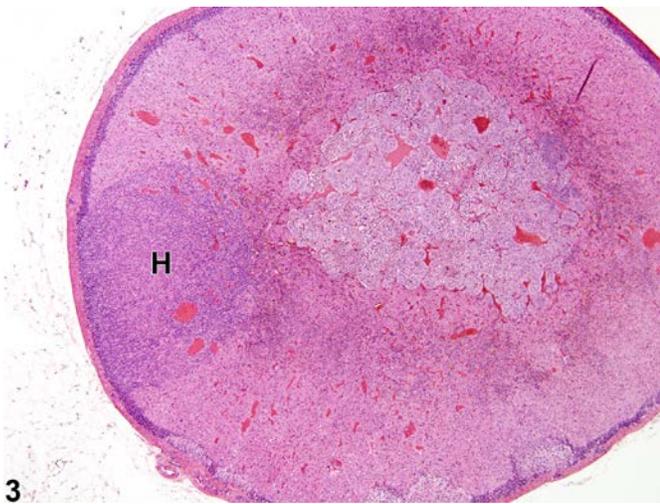
Adrenal Gland – Hyperplasia



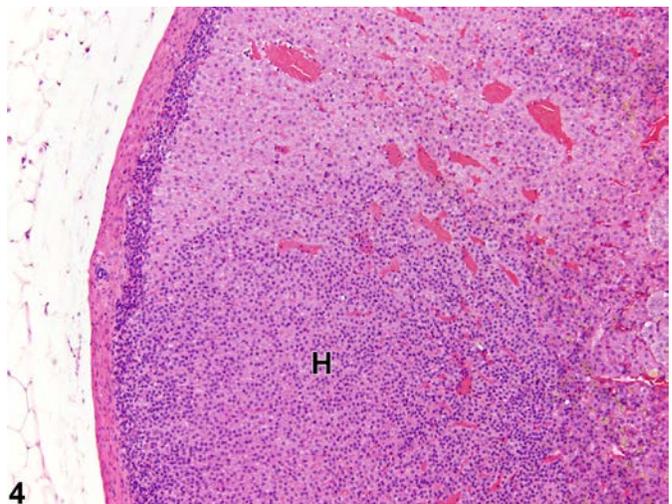
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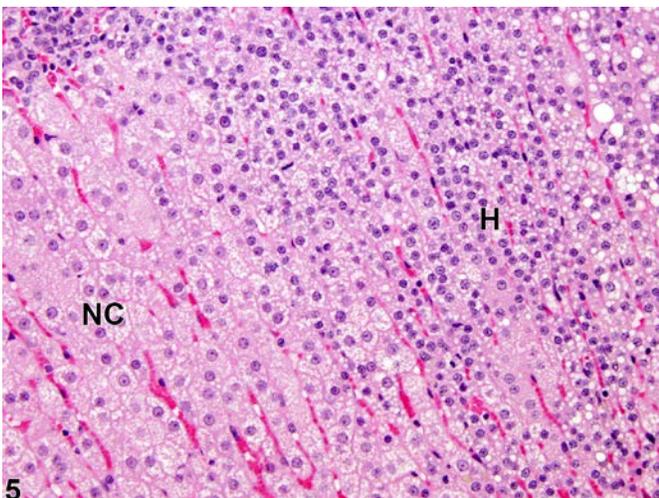
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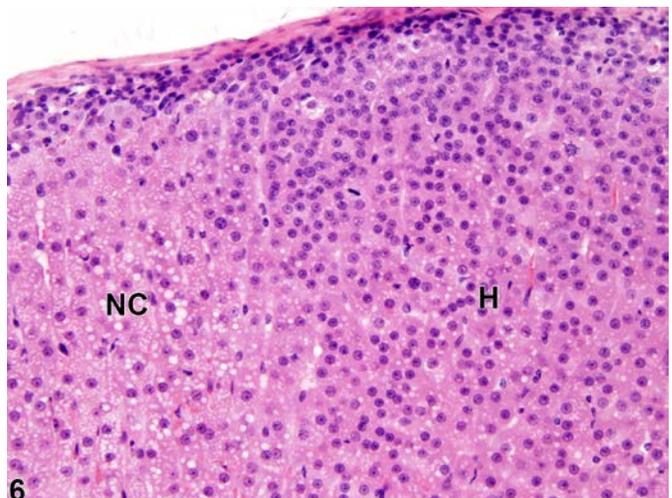
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Adrenal Gland – Hyperplasia

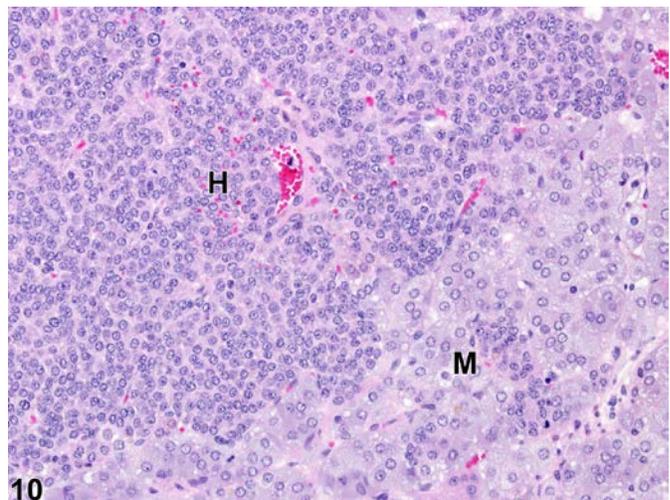
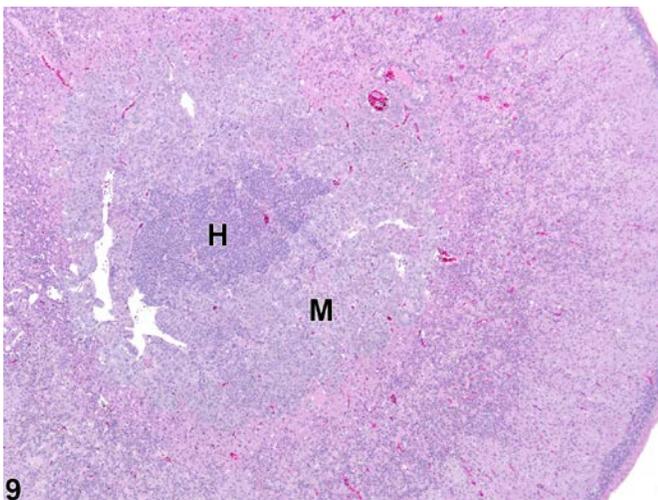
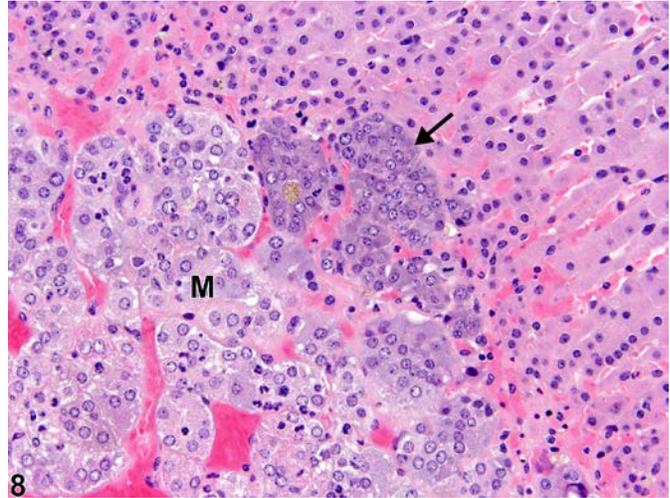
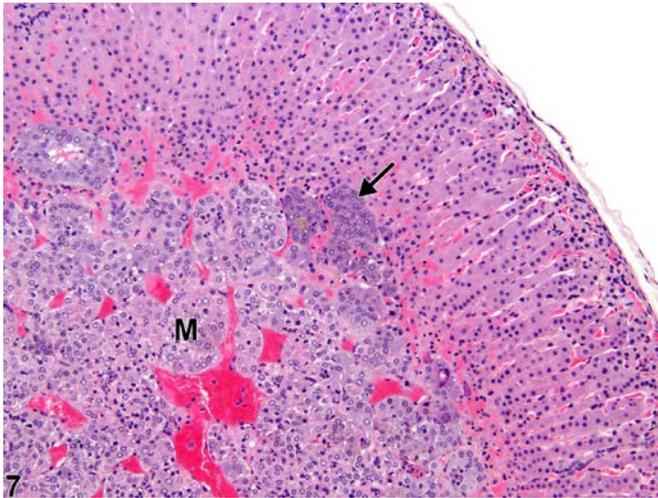


Figure Legend: **Figure 1** Adrenal gland, Cortex - Hyperplasia in a male Sprague-Dawley rat from a chronic study. There are two adjacent foci of hyperplasia (H) in the zona fasciculata. **Figure 2** Adrenal gland, Cortex - Hyperplasia in a male Sprague-Dawley rat from a chronic study (higher magnification of Figure 1). The foci of hyperplasia (H) are rounded, circumscribed areas of increased cellularity. **Figure 3** Adrenal gland, Cortex - Hyperplasia in a female Sprague-Dawley rat from a chronic study. There is a circumscribed but noncompressive focus of hyperplasia (H) in the zona fasciculata. **Figure 4** Adrenal gland, Cortex - Hyperplasia in a female Sprague-Dawley rat from a chronic study (higher magnification of Figure 3). The cells in this hyperplastic lesion (H) are smaller and more closely packed than those in the adjacent normal cortex. **Figure 5** Adrenal gland, Cortex - Hyperplasia in a female F344/N rat from a



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chronic study. There is a hyperplastic lesion (H) in which cortical cells are increased in number but are smaller in size than adjacent normal cortical cells (NC). **Figure 6** Adrenal gland, Cortex - Hyperplasia in a female F344/N rat from a chronic study. The hyperplastic lesion (H) has an increased number of cells that are smaller than adjacent normal cortical cells (NC). **Figure 7** Adrenal gland, Medulla - Hyperplasia in a male B6C3F1/N mouse from a chronic study. There is a small, noncompressive focus of hyperplastic medullary cells at the corticomedullary junction (arrow). M = medulla. **Figure 8** Adrenal gland, Medulla - Hyperplasia in a male B6C3F1/N mouse from a chronic study (higher magnification of Figure 1). The hyperplastic cells (arrow) are increased in number but are smaller and more basophilic than adjacent normal medullary cells (M). **Figure 9** Adrenal gland, Medulla - Hyperplasia in a male F344/N rat from a chronic study. There is focal hyperplasia (arrow) deep in the medulla (M). **Figure 10** Adrenal gland, Medulla - Hyperplasia in a male F344/N rat from a chronic study (higher magnification of Figure 9). The hyperplastic cells (H) are smaller (so the nuclei appear more crowded) and more basophilic than the adjacent normal medullary cells (M).

Comment: Hyperplasia is defined as a focal to diffuse increase in cell number. Hyperplasia is generally focal, though diffuse hyperplasia may occur. One or both adrenal glands can be affected. In both rats and mice, cortical hyperplasia most commonly occurs in the zona fasciculata (Figure 1, Figure 2, Figure 3, Figure 4, Figure 5, and Figure 6), though the zona reticularis can also be affected.

Hyperplastic foci in the cortex and medulla are generally rounded, circumscribed areas of variable diameter, characterized by increased numbers of cortical cells. In the cortex, the normal radial cord-like architecture is usually maintained. The hyperplastic foci can be well-demarcated or can blend almost imperceptibly with the adjacent normal tissue; compression is generally absent to minimal. Compared with normal cortical cells, hyperplastic cells are usually but not always smaller, with cytoplasm that can be vacuolated and/or tinctorially different (often more basophilic). In the medulla, foci of hyperplasia are often located at the periphery of the adrenal medulla, at or near the corticomedullary junction (Figure 7 and Figure 8), though they can also occur in the more central medulla (Figure 9 and Figure 10). Compared with normal medullary cells, hyperplastic cells are usually smaller with more basophilic cytoplasm (Figure 7, Figure 8, Figure 9, and Figure 10). In both the cortex and medulla, rare mitotic figures may be present, but the hyperplastic cells typically lack features of cellular atypia.



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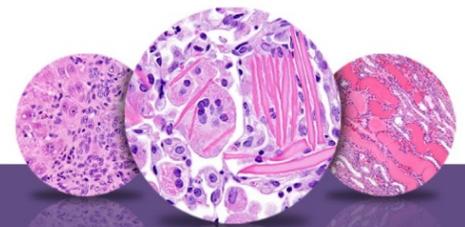
Adrenal Gland – Hyperplasia

Cortical and medullary hyperplasia can be a spontaneous aging change, which occurs more commonly in rats than mice. Other causes of cortical hyperplasia include stress, and abnormally elevated adrenocorticotrophic hormone (ACTH) levels due to any factor that perturbs the hypothalamic-pituitary-adrenal hormonal axis and/or adrenal steroidogenesis. Medullary hyperplasia can also result from experimental genetic modifications, dietary manipulations, and administration of various chemicals. Hyperplasia may also be a regenerative response to cell loss from degeneration, atrophy, or necrosis.

Focal cortical and medullary hyperplasias are considered proliferative lesions in a morphologic continuum that can progress to neoplasia (adenoma and carcinoma in the cortex and benign and malignant pheochromocytoma in the medulla). Differentiating large focal hyperplasias from smaller adenomas or pheochromocytomas can be challenging, but the neoplasms, compared with hyperplastic foci, are more compressive, exhibit more disorganization, and have some degree of cellular pleomorphism.

Cortical hyperplasia (increased cell numbers) and cortical hypertrophy (increased cell size) can often be concurrent lesions in the same gland or even in the same focus. Thus, as a practical matter, determining whether hyperplasia or hypertrophy is predominant in a given lesion and/or adrenal gland can be very difficult.

Recommendation: Adrenal gland - Hyperplasia should be diagnosed and assigned a severity grade and site modifier (i.e., cortex, medulla) and distribution modifier (i.e., focal, diffuse). The modifier “bilateral” should be added when hyperplasia is present in both glands. When there is focal hyperplasia and a neoplasm in the same site (cortex or medulla) in the same adrenal gland, both should be diagnosed only if the pathologist feels they are separate lesions; otherwise, only the neoplasm is diagnosed. In cases where cortical hyperplasia and hypertrophy are present in the same lesion, only hyperplasia should be diagnosed, with the hypertrophy described in the pathology narrative.



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Adrenal Gland – Hyperplasia

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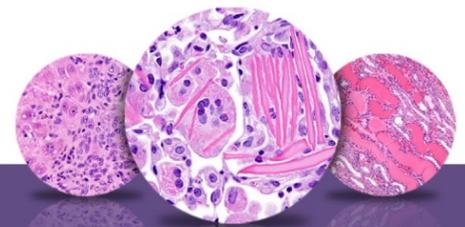
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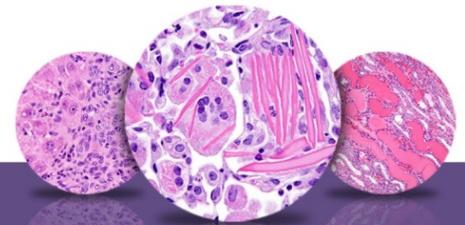


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